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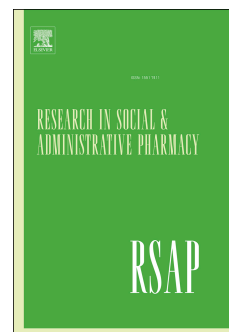
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# Accepted Manuscript

Medication administration errors and mortality: Incidents reported in England and Wales between 2007- 2016

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## **Medication administration errors and mortality: incidents reported in England and Wales between 2007–2016**

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## ABSTRACT

**Background:** Medication administration errors may contribute to patient mortality, thus additional understanding of such incidents is required.

**Objectives:** To analyse medication administration errors reported in acute care as resulting in death, to identify the drugs concerned, and to describe medication administration error characteristics (location of error, error type, patient's age) by drug group.

**Methods:** Medication administration errors reported in acute care in 2007– 2016 (n=517,384) were obtained from the National Reporting and Learning System for England and Wales. Incidents reported as resulting in death (n=229) were analysed. Drugs were classified by two researchers using the British National Formulary. Drug categories were described by medication administration errors' year, location, patient age, and error category based on the incidents' original classification.

**Results:** Errors were most often reported on wards (66.4%, n=152), and in patients aged over 75 years (41.5%, n=95). The most common error category was omitted medicine or ingredient (31.4%, n=72); most common drug groups were cardiovascular (20.1%, n=46) and nervous system (10.0%, n=23). Most errors in patients under 12 years concerned drugs to treat infection; cardiovascular drugs were most common among other age groups.

**Conclusions:** In order to prevent these most serious of medication administration errors, interventions should focus on avoiding dose omissions, and administration of drugs for patient over 75 years old, as well as safe administration of parenteral anticoagulants and antibacterial drugs.

**Keywords:** adverse event, death, drug, incident reporting, medication administration, patient safety

## Abbreviations

ADE = adverse drug event

BNF = British National Formulary

ISMP = Institute for Safe Medication Practices

MAE = medication administration error

NHS = National Health Service

NRLS = National Reporting & Learning System

## INTRODUCTION

In 2017, The World Health Organization (WHO) launched a third global patient safety challenge “Medication Without Harm”, aimed at improving medication safety, on the basis that medication errors are a leading cause of injury and avoidable harm in health care systems globally generating costs that has been estimated at 42 billion USD annually.<sup>1</sup> In February 2018, the report of the prevalence and burden of medication errors in England was published in response to the WHO challenge, estimating that 237 million medication errors at all stage of medication process occur in England per annum.<sup>2</sup>

The United States National Coordinating Council for Medication Error Reporting and Prevention<sup>3</sup> defines medication error as “any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer”. The medication administration stage of the medication process is known to be prone to errors. Half or more of all medication incidents are medication administration errors (MAEs).<sup>2 4 5</sup> MAEs can be defined as “a deviation from the prescriber’s medication order as written on the patient’s chart, manufacturers’ preparation/administration instructions, or relevant institutional policies”.<sup>6</sup> Direct observations of the inpatient medication process produce the most rigorous data on the prevalence of medication errors, and suggest that MAEs occur in 5% of non-intravenous and 35% of intravenous doses<sup>7</sup> or up to 20% of all doses given.<sup>8 9</sup> Fortunately, the majority of MAEs do not result in harm<sup>2 10</sup>, but some are serious or even fatal. An adverse drug event (ADE) is defined as “an injury resulting from medical intervention related to a drug”.<sup>11</sup>

Medication errors as well as ADEs during hospitalization are more likely in the presence of co-morbidity and polypharmacy,<sup>2 12</sup> and among older people.<sup>2 13</sup> Some drugs are more likely to cause significant patient harm when used in error. These are listed as high-alert medications by the US Institute for Safe Medication Practices (ISMP).<sup>14</sup> In acute care settings, these drug classes include anaesthetics, anti-arrhythmics, anti-thrombotics, chemotherapeutics, dialysis solutions, epidural or intrathecal medications, insulin, narcotics/opioids, and parenteral nutrition.<sup>14</sup> The UK’s high risk drug list includes administration of methotrexate, diamorphine and morphine injections, low molecular weight heparins, anticoagulants, insulin, lithium, midazolam injection, opioids, injectable medicines, and liquid medicines as well as omitted doses.<sup>15</sup> Additionally, a systematic review

revealed that 47 % of all serious medication errors were caused by seven drugs / drug classes. Those were methotrexate, warfarin, nonsteroidal anti-inflammatory drugs (NSAIDs), digoxin, opioids, acetylic salicylic acid, and beta-blockers.<sup>16</sup>

Analysis of reported medication errors have traditionally included all medication incidents, whether or not they result in harm<sup>4 5</sup>. By focussing on the most serious MAEs, the aim was to specifically study the characteristics of MAEs reported as resulting in patient death. This study's objectives were 1) to analyse medication administration errors reported in acute care as resulting in death, 2) to identify the drugs concerned, 3) to describe MAE characteristics by drug group, and 4) to identify potential areas for intervention.

## METHODS

### Design & setting

This was a retrospective study of MAEs reported to the National Reporting & Learning System (NRLS) for England and Wales. The NRLS collects national data on all patient safety incidents that are voluntarily and anonymously reported by staff employed in the National Health Services (NHS) and other health care organisations. Incidents (including near misses and incidents causing harm) can also be reported directly to the NRLS. Data reported for incidents include both categorical data (e.g. type, severity of incident) and a free text description of what happened.

The original classification of the NRLS incidents were used. Based on this classification, location of error included: ward, intensive care unit, operating theatre, recovery room, anaesthetic room, therapy department, pharmacy, mortuary, hospital buildings, other, or the information was missing. Types of errors were: omitted medicine / ingredient, wrong / unclear dose or strength, wrong drug / medicine, wrong frequency, wrong quantity, wrong route, adverse drug reaction (when used as intended), patient allergic to treatment, contra-indication to the use of the medicine in relation to drugs or conditions, mismatching between patient and medicine, wrong storage, wrong method of preparation / supply, wrong / omitted verbal patient directions, wrong / omitted / passed expiry date, other, or unknown.

## Data acquisition

A data sharing agreement was signed after applying and receiving acceptance from NRLS for data access. NRLS extracted the data (medication administration errors reported to the NRLS between 1 January 2007 and 31 December 2016) in December 2017. Inclusion criteria were that the incident was documented as involving: 1) medication, 2) administration / supply of a medicine from a clinical area, and 3) acute NHS trust (either a specialist or non-specialist organisation). Of all incidents (n=517,384), 94.3% concerned an acute non-specialist Trust, and only 5.7% acute specialist Trust. The total number of incidents extracted was 517,384. Of these, only MAEs reported as resulting in death caused by a patient safety incident (n=229, 0.04%) were analysed. Only the categorical data fields within the NRLS data were acquired.

## Data analysis

Descriptive statistics of the data (n=229 MAEs reported as resulting in death) were calculated using IBM SPSS (version 23.0). Characteristics of the data were described using frequencies and percentages, and relationships amongst factors explored via cross-tabulation. Reports including the name of the drug were classified using the British National Formulary (BNF) classification.<sup>17</sup> The BNF classification's main groups are divided under the following sections: 1. Gastro-intestinal system, 2. Cardiovascular system, 3. Respiratory system, 4. Nervous system, 5. Infection, 6. Endocrine system, 7. Genito-urinary system, 8. Malignant disease, 9. Blood and nutrition, 10. Musculoskeletal system, 11. Eye, 12. Ear, nose, and oropharynx, 13. Skin, 14. Vaccines, 15. Anaesthesia, and 16. Emergency treatment of poisoning. MH classified the drugs into BNF groups which were then verified by BDF. Drug categories were cross-tabulated by MAEs' year, location, patients' age, and error category. The age bands used within the NRLS were amalgamated into six broader groups: 1) under 12 years, 2) 12-17 years, 3) 18-25 years, 4) 26-55 years, 5) 56-75 years, and 6) over 75 years.

## **Ethics**

King's College London ethics committee approved the study (LRS-17/18-5150). The data did not include any personal or organisational identifiers, thus anonymity of the reporters, patients, other involved persons, and organisations could be guaranteed.

## **RESULTS**

### **Characteristics of MAEs resulting in death**

MAEs resulting in death (n=229) occurred most often in 2008 (n=28, 12.2% of all MAEs reported as causing death) and 2016 (n=28, 12.2%), and less often 2012 (n=13, 5.7%). Overall 66.4% of MAEs were reported as occurring on non-critical care wards, and 41.5% (n=95) occurred amongst patients aged over 75 years. The most common error category was omitted medicine or ingredient (n=72, 31.4%). (Table 1.)

### **Drugs related to MAEs**

The name of the related drug was mentioned in 58.1% (n=133) of all MAEs. The most common group of drugs in MAEs reported as resulting in death were cardiovascular drugs (20.1%, n=46). Of these 26 involved parenteral anticoagulants, six oral anticoagulants, and six sympathomimetics. The second most common were drugs of the central nervous system (10.0%, n=23). Of those, analgesics (n=10) were most common. Other common drug groups were antibacterials (n=20), cytotoxic drugs (n=8), and insulin (n=7). (Tables 2.) More specific information by name of drugs concerned (as written in the reports) is presented in Table 3.

### **MAE characteristics by drug groups**

MAEs reported as resulting in death in general ward areas were most often reported for cardiovascular drugs (34 cases of 152 incidents at ward) followed by nervous systems drugs



(19 of 152). MAEs occurring in intensive care units most commonly concerned drugs used in blood and nutrition (4 of 18 incidents in intensive care units) and infection (3 of 18). Most MAEs in patients under 12 years were drugs to treat infection (3 of 10 incidents in patients under 12 years) whereas for patient's aged 26-55 years cardiovascular drugs (6 of 29 incidents in patients aged 26-55 years) were the most common. Cardiovascular drugs (9 of 58 of incidents in patients aged 56-75) or drugs to treat infection (10 of 58) featured most often for patients aged 56-75, and cardiovascular drugs (23 of 95 incidents in patients aged over 75 years) and nervous system drugs (11 of 95) for patients aged over 75. (Online appendix.)

The most common error categories for cardiovascular drugs were omitted medicine / ingredients (18 of 46 incidents with cardiovascular drugs), followed by wrong / unclear dose or strength (6 of 46). For nervous system drugs the most commonly reported errors were wrong / unclear dose or strength (4 of 23 incidents with nervous system drugs), wrong quantity (3 of 23), and wrong drug / medicine (3 of 23). For drugs to treat infection the most commonly reported errors were omitted medicine /ingredient (5 of 21 incidents with drugs to treat infection), adverse drug reaction (4 of 21), and patient allergic to treatment (4 of 21). (Online appendix.)

## DISCUSSION

In this study, MAEs most commonly reported as causing mortality in acute care Trusts over the 10-year period 2007 to 2016 were omissions of drugs. They occurred more often on hospital wards than other locations and amongst patients aged over 75 years. The drugs most commonly involved were parenteral anticoagulants followed by antibacterial drugs. Interventions to reduce MAEs, should therefore focus on those areas.

Almost one third of MAEs were related to omissions of drug doses. A previous study analysing all medication errors reported to the NRLS between 2005 and 2010 also found that omissions were the most commonly reported type, accounting for around 15% of incidents,<sup>4</sup> which is much lower than in the present study. In addition, a previous systematic review using observational evidence demonstrated that omission errors are the most common MAE type internationally.<sup>18</sup> More attention is needed on omissions since the

consequences can be serious. The risks of delay or omission of drugs have been categorised by the English National Patient safety Agency (NPSA),<sup>19</sup> which suggests that omission of anticoagulants, insulins, and cytotoxic agents, as identified in this study, can cause significant or catastrophic long-term patient impact. Reasons for medication omissions are manifold, such as staff shortages and delays in medication dispensing,<sup>20</sup> patients' inability to take the medicine, or medication unavailability.<sup>21</sup> More active solutions for problems related to medication omissions should be implemented with the development of technology, improving work processes, flow of information, verification systems and availability of drugs. Still, it is challenging to recommend any specific interventions, as a previous systematic review and meta-analysis demonstrated that interventions developed to decrease MAEs, including nurse training and education, automated delivery systems and barcode-assisted medication administration systems, did not find clear effect of the interventions.<sup>22</sup>

Cardiovascular drugs, particularly parenteral anticoagulants, were the most common drug group involved in MAEs reported as resulting in death. Many of those were omitted or administered in the wrong dose, strength, frequency, or quantity. Cardiovascular drugs were associated with the highest median proportion of preventable adverse drug reactions (PADR) also in a previous review of systematic reviews of inpatients' PADRs<sup>23</sup>. Those were also found to be the most frequent types of drugs involved in preventable ADEs<sup>24</sup>, and commonly related to observed MAEs<sup>18</sup>. Similarly, heparin and low molecular weight heparin were amongst the most common drugs reported as causing death in other previous studies,<sup>4 5</sup> demonstrating that the consequences of an error are more devastating for patients receiving these types of drugs as there is only a narrow difference between an effective and a toxic dose.<sup>5</sup> In addition, omission of such drugs may have a significant or catastrophic long-term impact<sup>19</sup> and the risk of ADEs has been found to increase especially for inpatients with coronary disease and using related drugs.<sup>12</sup> Thus, efforts to avoid dose omissions should focus on these patients.

Antibacterial drugs were also a common group of drugs identified in the present study. Most MAEs related to these drugs were omissions, adverse drug reactions, and administration to patients with a documented allergy. These drugs have been previously found to be related to medication errors causing death,<sup>4</sup> but are not amongst ISMP's list of

high-alert medications.<sup>14</sup> The data in the present study show that patients' allergies and other adverse reactions of drugs may not be verified as carefully as required. Other common drugs related to patients' deaths were opioids, insulins, and cytotoxic drugs, all in ISMP's list of high-alert medications<sup>14</sup>. The most common error types for nervous systems drugs (including opioids) were wrong or unclear dose or strength, wrong drug, or wrong quantity. Further research is needed to understand the reasons for these error types.

Each death caused by medication error is one death too many. There should also be some focus on rare and unusual MAEs. For example two MAEs resulting in death were caused by the administration of potassium permanganate (orally instead of topically). An NPSA Patient Safety Alert produced in 2014 was based on death caused by a patient ingesting potassium permanganate.<sup>25</sup> One incident in our data occurred before this alert and another afterwards, in 2016. More knowledge and competence in handling drugs and administration of drugs should be provided to all health professionals, especially nurses, as they are usually the final step in the medication use process. Educating patients about the medications they are receiving may help to reduce MAEs.

### **Strengths and limitations**

This study was of a sufficient size to be able to identify rare MAEs that result in death. Drugs were classified into BNF category by two researchers, which supports reliability and validity. It is known that reported incidents do not represent all those that occur, and it is assumed that self-reporting systems (such as the NRLS) detect only a very small proportion of all medication incidents<sup>2</sup>. The incident reporting system has further possible weaknesses in that reporters may evaluate the consequences of incidents incorrectly such that some of the MAEs reported as resulting in death incidents may allude to possible rather than actual consequences. It was only possible to identify the name of the drug for 56% of all reports and only the categorical fields from the NRLS data were used in this analysis. In addition, the original classification of NRLS incidents was used, and it is thus impossible to evaluate what error types are hidden under the 'other' category. A further issue is whether an 'adverse drug reaction' may be an MAE when medication is administered for the first time to the patient, but descriptions of reported incidents did not include enough information to allow

re-classification. The free text descriptions could have provided a more detailed understanding of each incidents and further information about the drugs involved.

## CONCLUSION

In order to prevent the most serious MAEs, additional studies and interventions should focus on dose omissions and administration of drugs to patients over 75 years old, as well as safe administration of parenteral anticoagulants and antibacterial drugs. Checking patient allergies and undertaking required verification procedures before medication administration, as well as additional education for safe handling and administration of drugs should be mandatory. Additional studies using observational research methods are important for exploring further the dynamics of serious MAEs.

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## REFERENCES

1. WHO. Medication Without Harm: WHO's Third Global Patient Safety Challenge. <http://www.who.int/patientsafety/medication-safety/en/> 2018 Accessed 06.06.18
2. Elliott RA, Camacho E, Campbell F, Jankovic D, Martyn St James M, Kaltenthaler E, Wong R, Sculpher MJ, Faria R. Prevalence and economic burden of medication errors in the NHS in England. Rapid evidence synthesis and economic analysis of the prevalence and burden of medication error in the UK. Policy Research Unit in Economic Evaluation of Health & Care Interventions (EEPRU). <http://www.eepru.org.uk/wp-content/uploads/2018/02/eepru-report-medication-error-feb-2018.pdf> 2018 Accessed 14.06.18
3. NCCMERP. The National Coordinating Council for Medication Error Reporting and Prevention. Medication errors – Definition. <http://www.nccmerp.org/about-medication-errors> 2018 Accessed 18.05.18
4. Cousins DH, Gerrett D, Warner B. A review of medication incidents reported to the National Reporting and Learning System in England and Wales over 6 years (2005-2010). *Br J Clin Pharmacol*. 2012;74:597-604.
5. ISMP Canada. Ontario Hospital Critical Incidents Related to Medications or IV Fluids Analysis Report. October 2011 to December 2012. [http://www.ismp-canada.org/download/ocil/ON\\_Critical\\_Incidents\\_Analysis\\_Report\\_31May2013.pdf](http://www.ismp-canada.org/download/ocil/ON_Critical_Incidents_Analysis_Report_31May2013.pdf) 2018 Accessed 06.06.18
6. Keers RN, Williams SD, Cooke J, Ashcroft DM. Prevalence and Nature of Medication Administration Errors in Health Care Settings: A systematic Review of Direct Observational Evidence. *Ann Pharmacother*. 2013;47:237-256.
7. McLeod MC, Barber N, Franklin BD. Methodological variations and their effects on reported medication administration error rates. *BMJ Qual & Saf*. 2013;22:278-89
8. Keers RN, Williams SD, Cooke J, Ashcroft DM. Causes of medication administration errors in hospitals: a systematic review of quantitative and qualitative evidence. *Drug Saf*. 2013;36:1045-67.
9. Härkänen M, Ahonen J, Kervinen M, Turunen H, Vehviläinen-Julkunen K. The factors associated with medication errors in adult medical and surgical inpatients: a direct observation approach with medication record reviews. *Scand J Caring Sci*. 2015;29:297-306.
10. Maaskant J, Bosman D, van Rijn-Bikker P, van Aalderen W, Vermeulen H. Preventable errors with non-opioid analgesics and antiemetic drugs may increase burden in surgical pediatric patients. *Eur J Pediatr Surg*. 2014;24:381-8.
11. Kohn LT, Corrigan JM, Donaldson MS, editors. *To Err is Human: Building a Safer Health System*. Institute of Medicine (US) Committee on Quality of Health Care in America;. Washington (DC): National Academies Press (US); 2000.

- 302 12. Härkänen M, Kervinen M, Ahonen J, Voutilainen A, Turunen H, Vehviläinen-Julkunen K.  
 303 Patient-specific risk factors of adverse drug events in adult inpatients – evidence detected  
 304 using the Global Trigger Tool method. *J Clin Nurs*. 2015;24(3-4):582-91.
- 305 13. Haukland EC, von Plessen C, Nieder C, Vonnen B. Adverse events in hospitalised cancer  
 306 patients: a comparison to a general hospital population. *Acta Oncol*. 2017;56:1218-1223.
- 307 14. ISMP. High-Alert Medications in Acute Care Settings. July 25, 2014.  
 308 [https://www.ismp.org/sites/default/files/attachments/2018-](https://www.ismp.org/sites/default/files/attachments/2018-01/highalertmedications%281%29.pdf)  
 309 [01/highalertmedications%281%29.pdf](https://www.ismp.org/sites/default/files/attachments/2018-01/highalertmedications%281%29.pdf) 2018 Accessed 06.06.18
- 310 15. National Patient Safety Agency: High Risk Drugs List.  
 311 [http://www.sssft.nhs.uk/images/pharmacy/documents/high\\_risk\\_drugs\\_list/High-Risk-](http://www.sssft.nhs.uk/images/pharmacy/documents/high_risk_drugs_list/High-Risk-Drugs-List.pdf)  
 312 [Drugs-List.pdf](http://www.sssft.nhs.uk/images/pharmacy/documents/high_risk_drugs_list/High-Risk-Drugs-List.pdf) 2018 Accessed 29.10.18
- 313 16. Saedder EA, Brock B, Nielsen LP, Bonnerup DK, Lisby M. Identifying high-risk medication:  
 314 a systematic literature review. *Eur J Clin Pharmacol*. 2014;70(6):637-45.
- 315 17. BNF 70. September 2015 – March 2016.  
 316 [file:///C:/Users/marhar/Documents/Data%20mining%20-%20incidents/british-national-](file:///C:/Users/marhar/Documents/Data%20mining%20-%20incidents/british-national-formulary-2015.pdf)  
 317 [formulary-2015.pdf](file:///C:/Users/marhar/Documents/Data%20mining%20-%20incidents/british-national-formulary-2015.pdf) 2018 Accessed 15.06.18
- 318 18. Keers RN, Williams SD, Cooke J, Ashcroft DM. Prevalence and nature of medication  
 319 administration errors in health care settings: a systematic review of direct observational  
 320 evidence. *Ann Pharmacother*. 2013;47(2):237-56.
- 321 19. NPSA Rapid Response Report: Reducing Harm from omitted and delayed medicines in  
 322 hospital A tool to support local implementation.  
 323 <http://www.ukmi.nhs.uk/filestore/ukmiaps/RRR09-UKMItool.pdf> 2018 Accessed 06.06.18
- 324 20. Leite B, Mistro S, Carvalho C, Mehta SR, Badaro R. Cohort study for evaluation of dose  
 325 omission without justification in a teaching general hospital in Bahia, Brazil. *Int J Qual Health*  
 326 *Care*. 2016;28:288-93.
- 327 21. Shandilya S, Nizamuddin K, Faisal MW, Noor S, Abraham S. Omitted medications: a  
 328 continuing problem. *Clin Med (Lond)*. 2015;15:12-4.
- 329 22. Berdot S, Roudot M, Schramm C, Katsahian S, Durieux P, Sabatier B. Interventions to  
 330 reduce nurses' medication administration errors in inpatient settings: A systematic review  
 331 and meta-analysis. *Int J Nurs Stud*. 2016;53:342-50.
- 332 23. Wolfe D, Yazdi F, Kanji S, Burry L, Beck A, Butler C, Esmaeilisaraji L, Hamel C, Hersi M,  
 333 Skidmore B, Moher D, Hutton B. Incidence, causes, and consequences of preventable  
 334 adverse drug reactions occurring in inpatients: A systematic review of systematic reviews.  
 335 *PLoS One*. 2018;13(10): e0205426.

336 24. Jolivot PA, Pichereau C, Hindlet P, Hejblum G, Bigé N, Maury E, Guidet B, Fernandez C.  
337 An observational study of adult admissions to a medical ICU due to adverse drug events.  
338 Ann Intensive Care. 2016;6(1):9.

339 25. NHS. Patient Safety Alert. Stage One: Warning. Risk of death or serious harm from  
340 accidental ingestion of potassium permanganate preparations. 22 December 2014  
341 <https://www.england.nhs.uk/wp-content/uploads/2014/12/psa-potass-prmangant.pdf>  
342 2018 Accessed 03.06.18

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347 Table 1. Characteristics of medication administration incidents resulting in death (n=229)

Variable	No.	%
<b>Year</b>		
- 2007	23	10.0
- 2008	28	12.2
- 2009	19	8.3
- 2010	22	9.6
- 2011	26	11.4
- 2012	13	5.7
- 2013	25	10.9
- 2014	24	10.5
- 2015	21	9.2
- 2016	28	12.2
<b>Location</b>		
- Ward	152	66.4
- Intensive care unit / high dependency unit	18	7.9
- Operating theatre	10	4.4
- Other	4	1.7
- Recovery room	2	0.9
- Hospital buildings (inside)	2	0.9
- Therapy department	2	0.9
- Pharmacy	1	0.4
- Anaesthetic room	1	0.4
- Mortuary	1	0.4
- Missing information	36	15.7
<b>Patient's age</b>		
- under 12	10	4.4
- 12-17	0	0.0
- 18-25	2	0.9
- 26-55	29	12.7
- 56-75	58	25.3
- over 75	95	41.5
- Missing	35	15.2
<b>Medication error category</b>		
- Omitted medicine / ingredient	72	31.4
- Other	37	16.2
- Wrong / unclear dose or strength	24	10.5
- Adverse drug reaction (when used as intended)	21	9.2
- Wrong drug / medicine	16	7.0
- Wrong frequency	13	5.6
- Wrong quantity	13	5.6
- Wrong route	8	3.5
- Patient allergic to treatment	7	3.1
- Contra-indication to the use of the medicine in relation to drugs or conditions	5	2.2
- Mismatching between patient and medicine	3	1.3
- Unknown	3	1.3
- Wrong storage	2	0.9
- Wrong method of preparation / supply	2	0.9
- Wrong / omitted verbal patient directions	2	0.9
- Wrong / omitted / passed expiry date	1	0.4

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Table 2. Classified drugs related to death causing medication administration incidents  
(n=229)

BNF Drug classes	No.	%
<b>1. Gastro-intestinal system</b>	0	0.0
<b>2. Cardiovascular system</b> - 2.2 (n=1) Diuretics - 2.3 (n=2) Anti-Arrhythmic Drugs - 2.5 (n=2) Hypertension and Heart Failure - 2.7 (n=6) Sympathomimetic - 2.8 (n=26) Parenteral Anticoagulants, (n=6) Oral Anticoagulants - 2.10 (n=1) Stable Angina, Acute/Coronary Synd&Fibrin - 2.11 (n=2) Antifibrinolytic Drugs & Haemostatics	46	20.1
<b>3. Respiratory system</b> - 3.6 (n=2) Oxygen	2	0.9
<b>4. Nervous system</b> - 4.1 (n=3) Hypnotics And Anxiolytics - 4.2 (n=1) Drugs Used In Psychoses & Rel.Disorders - 4.3 (n=1) Antidepressant Drugs - 4.6 (n=1) Drugs Used In Nausea And Vertigo - 4.7 (n=10) Analgesics - 4.8 (n=6) Antiepileptic Drugs - 4.9 (n=1) Drugs Used In Parkinsonism/Related Disorders	23	10.0
<b>5. Infection</b> - 5.1 (n=20) Antibacterial Drugs - 5.3 (n=1) Antiviral Drugs	21	9.2
<b>6. Endocrine system</b> - 6.1.1 (n=7) Insulin - 6.3 (n=1) Corticosteroids (Endocrine)	8	3.5
<b>7. Genito-urinary system</b>	0	0.0
<b>8. Malignant disease</b> - 8.1 (n=8) Cytotoxic Drugs - 8.2 (n=1) Drugs Affecting The Immune Response	9	3.9
<b>9. Blood and nutrition</b> - 9.1 (n=1) Anaemias + Other Blood Disorders - 9.2 (n=4) Fluids And Electrolytes - 9.3 (n=2) Intravenous Nutrition - 9.5 (n=4) Minerals	11	4.8
<b>10. Musculoskeletal system</b> - 10.2 (n=1) Drugs Used In Neuromuscular Disorders	1	0.4
<b>11. Eye</b> - 11.8 (n=1) Miscellaneous Ophthalmic Preparations	1	0.4
<b>12. Ear, nose, and oropharynx</b>	0	0.0
<b>13. Skin</b> - 13.11 (n=3) Skin Cleansers, Antiseptics & Desloughing	3	1.3
<b>14. Vaccines</b>	0	0.0
<b>15. Anaesthesia</b> - 15.1 (n=1) General Anaesthesia	1	0.4
<b>16. Emergency treatment of poisoning</b>	2	0.9
Multiple	2	0.9
Other	3	1.3
Missing	96	41.9
<b>Total</b>	<b>229</b>	<b>100</b>

Table 3. Names of the drugs related to death causing incidents (as written in reports)

BNF code	Drug names (as written in incident reports)
<b>2. Cardiovascular system</b>	
2.2 Diuretics	bumetanide
2.3 Anti-Arrhythmic Drugs	Digoxin [digitalis], amiodarone
2.5 Hypertension and Heart Failure	doxazosin and ramipril, verapamil
2.7 Sympathomimetic	noradrenaline x6, adrenaline x2, isoprenaline, metaraminol
2.8 Parenteral Anticoagulants & Oral Anticoagulants	enoxaparin x 7, Clexane [enoxaparin] x 6, heparin x 6, tinzaparin x 3, Fragmin [dalteparin sodium] x 4, warfarin x 3, rivaroxiban x 2, apixaban
2.10 Stable Angina, Acute/Crnry Synd&Fibrin	alteplase
2.11 Antifibrinolytic Drugs & Haemostatics	factor VIII, vitamin K
<b>3. Respiratory system</b>	
3.6 Oxygen	oxygen x 2
<b>4. Nervous system</b>	
4.1 Hypnotics And Anxiolytics	midazolam x 2, lorazepam
4.2 Drugs Used In Psychoses & Rel.Disorders	haloperidol
4.3 Antidepressant Drugs	mirtazapine
4.6 Drugs in Nausea And Vertigo	prochlorperazine / cyclizine,
4.7 Analgesics	aspirin, oxycodone x 3, fentanyl, remifentanyl, morphine x 2, diamorphine, buprenorphine
4.8 Antiepileptic Drugs	phenytoin x 4, phenobarbital, thiopentone
4.9 Park'ism/Related Disorders	co-careldopa
<b>5. Infection</b>	
5.1 Antibacterial Drugs	co-amoxiclav x 4, gentamicin x 3, Augmentin [amoxicillin and clavulanate] x 3, Tazocin [piperacillin sodium /tazobactam sodium] x 2, cefuroxime, flucloxacillin x2, daptomycin, benzylpenicillin, rifampicin, trimethoprim, levofloxacin, linezolid
5.3 Antiviral Drugs	abacavir
<b>6. Endocrine system</b>	
6.1.1 Insulin	insulin x 7
6.3 Corticosteroids (Endocrine)	hydrocortisone
<b>8. Malignant disease</b>	
8.1 Cytotoxic Drugs	chemotherapy x 2, cyclophosphamide x 2, eribulin, vinorelbine, ifosfamide, bleomycin
8.2 Immune Response Drugs	alemtuzumab
<b>9. Blood and nutrition</b>	
9.1 Anaemias + Blood Disorders	iron dextran
9.2 Fluids And Electrolytes	potassium chloride x2, 0.9% normal saline 1000ml, sando K
9.3 Intravenous Nutrition	glucose, Vamin [amino acids]
9.5 Minerals	magnesium x2, calcium chloride x 2
<b>10. Musculoskeletal system</b>	
10.2 Drugs In Neuromusc. Disord.	pyridostigmine
<b>11. Eye / Miscellaneous Ophthalmic Preparations</b>	fluorescein
<b>13. Skin</b>	
13.11 Clean., Antisep. & Desloughing	chlorhexidine, potassium permanganate
<b>15. Anaesthesia</b>	
15.1 General Anaesthesia	atropine
<b>16. Emerg. treatment of poisoning</b>	flumazenil, protamine sulphate

## Online appendix. Medication administration incidents (n=229) characteristics by drug groups

BNF Drug classes	2. Cardio-vascular system	3. Respi-ratory system	4. Nervous system	5. Infec-tion	6. Endocrine system	8. Malignant disease	9. Blood and nutrition	10. Musculo-skeletal system	11. Eye	13. Skin	15. Anaest-hesia	16. Emergency treatment	Missing / other multiple	TOTAL
<b>Charecteristics</b>														
<b>Incidents' location</b>														
Ward	34	1	19	11	6	5	5	1	0	2	1	2	65	152
Intensive care unit	3	0	1	3	1	0	4	0	0	0	0	0	6	18
Operating theatre	0	0	1	2	0	0	0	0	0	1	0	0	6	10
Other	2	0	0	1	0	0	0	0	0	0	0	0	1	4
Recovery room	0	0	1	0	0	0	0	0	0	0	0	0	1	2
Hospital buildings	0	0	0	0	0	2	0	0	0	0	0	0	0	2
Therapy depart.	0	0	0	0	0	0	0	0	0	0	0	0	2	2
Pharmacy	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Anaesthetic room	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Mortuary	1	0	0	0	0	0	0	0	0	0	0	0	0	1
Missing	6	1	1	4	1	2	2	0	1	0	0	0	18	36
TOTAL	46	2	23	21	8	9	11	1	1	3	1	2	101	229
<b>Patient's age</b>														
under 12	2	0	1	3	0	0	2	0	0	0	0	0	2	10
18-25	0	0	1	0	0	0	0	0	0	0	0	0	1	2
26-55	6	0	3	1	0	2	1	0	0	0	0	1	15	29
56-75	9	1	3	10	0	5	4	0	0	1	1	0	24	58
over 75	23	1	11	4	5	1	3	1	0	2	0	1	43	95
Missing	6	0	4	3	3	1	1	0	1	0	0	0	16	35
TOTAL	46	2	23	21	8	9	11	1	1	3	1	2	101	229
<b>Error Category</b>														
Omitted medicine / ingredient	18	0	2	5	2	1	5	1	0	0	0	1	37	72
Other	4	0	2	0	3	2	1	0	0	0	1	1	23	37
Wrong / unclear dose or strength	6	1	4	0	1	2	2	0	0	0	0	0	8	24
Adverse drug reaction (when used as intended)	2	0	1	4	0	1	1	0	1	1	0	0	10	21
Wrong drug / medicine	4	0	3	1	1	0	0	0	0	0	0	0	7	16
Wrong frequency	3	0	1	1	0	1	1	0	0	0	0	0	6	13

Wrong quantity	4	1	3	1	0	0	1	0	0	0	0	0	3	13
Wrong route	2	0	1	0	0	1	0	0	0	2	0	0	2	8
Patient allergic to treatment	0	0	0	4	0	0	0	0	0	0	0	0	3	7
Contra-indication ..	1	0	1	2	0	1	0	0	0	0	0	0	0	5
Mismatching	1	0	1	1	0	0	0	0	0	0	0	0	0	3
Unknown	0	0	3	0	0	0	0	0	0	0	0	0	0	3
Wrong storage	0	0	0	1	0	0	0	0	0	0	0	0	1	2
Wrong preparation	0	0	0	0	1	0	0	0	0	0	0	0	1	2
Wrong verbal patient directions	0	0	1	1	0	0	0	0	0	0	0	0	0	2
Wrong / omitted / passed expiry date	1	0	0	0	0	0	0	0	0	0	0	0	0	1
TOTAL	46	2	23	21	8	9	11	1	1	3	1	2	101	229